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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/051,034	03/31/1998	IAN FARQUHAR CAMPBELL MCKENZIE	3164.98USWO	7533

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	45

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/051,034	MCKENZIE ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *43*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on December 22, 2003 has been entered.

DETAILED ACTION

This application is a 371 national stage filing of PCT/AU97/00492, filed August 1, 1997, which claims benefit of 60/024,279, filed August 21, 1996.

Claims 36-55 are pending and currently under examination.

Information Disclosure Statement

The information disclosure statement filed December 22, 2003, paper number 43, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Specifically, only the first page of each of the references was provided with the filing of the IDS. Unless otherwise indicated, only the first page of each of the cited references was considered. As indicated on the copy of the IDS, the references have

been considered only to the extent of the first page and the remaining material and information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claims 48 and 49 recite in step (a) "transducing the cells with a chimeric enzyme" however this inconsistent with step (b) in which the chimeric enzyme is expressed because an enzyme is not expressed. More clearly indicating in step (a) the specifics of how and with what the cells are transduced would address the basis of the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 36-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sandrin *et al.* (WO 95/34202) or Cooper *et al.* (6,331,658) with Sandrin *et al.* (Nature Med, Dec. 1995), Machamer (Curr. Opin. Cell Biol., 1993) and Sandrin *et al.*(Xenotransplantation, 1994).

Claims 36 and 37 encompass polynucleotide sequences that encode a chimeric enzyme comprising (1) a Golgi localization sequence, specifically from the alph-1,3 galactosyltransferase and (2) a catalytic domain of a fucosyl transferase. Dependent claims set forth specific domains and sequences for each of these two embodiments. At the time of filing it was known that the major antigen in the hyperacute rejection (HAR) of xenografts was the carbohydrate added by the alpha-1,3 galactosyl transferase enzyme. It was proposed and demonstrated by Sandrin *et al.* (WO 95/34202) or Cooper *et al.* (6,331,658) that the HAR carbohydrate antigen could reduce by expressing other transfer eases that altered the final carbohydrate. In particular, each teach the use of fucosyltransferase because it uses the same carbohydrate acceptor as the alpha-1,3 galactosyl transferase and provides for the O-blood type group (Sandrin *et al.* page 15 and Cooper *et al.* column 11, lines 25-40 and claim 4 for example). In addition, Sandrin *et al.* teach that the sequence of the fucosyl transferase expressed can be modified and comprise alterations to provide a functional transferase (page 15) which can be tested for its suitability with standard methods known in the art (page 16). At the time of filing the processing of carbohydrate structures/antigens on proteins by glcosyltransferases as it proceeded through the Golgi had been characterized. More specifically, Machamer in reviewing the state of the art provides an outline for post-translational modification of a protein wherein different transferases are present throughout a Golgi structure wherein there localization determined by targeting and retention sequences determines the specific carbohydrate structure attached to the protein as it proceeds

through and is processed in the Golgi. Evidence provided by Sandrin *et al.* and Cooper *et al.* clearly demonstrate that expression of fucosyltranferase in the Golgi provides for a means to reduce the amount of HAR antigen produced by the alpha-1,3 galactosyl transferase. Given the teaching that any functional fragment of the transferase can be used it would have been obvious that the polynucleotide sequences must encode a transferase that is localized in the Golgi, thus a functional transferase require a Golgi localization signal. Sandrin *et al.* (1995) specifically outline mechanisms for the results such competition in the Golgi for the same carbohydrate acceptor substrate noting the specific location of the fucosyltranferase and galactosyltransferase enzymes (page 1265, second column) and provide details to test and increase the affect of the localization to increase the substrate competition in the Golgi (page 1266). Sandrin *et al.* (1994) provide a disclosure of the mouse, human and pig sequences known at the time of filing and detail a specific description and comparison of the targeting domain sequences of each of the encoded galactosyltransferases. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to provide a sequences that encodes a fucosyltransferase that when expressed would be present in the Golgi. One having ordinary skill in the art would have been motivated to substitute the galactosyltransferase targeting domain onto a catalytically functional fucosyltransferase to provide for the same Golgi localization and more effective competition for the same carbohydrate acceptor. There would have been a reasonable expectation of success given the level of skill in the art to manipulate polynucleotide sequences to effectively provide a vector that could be used to express a chimeric enzyme containing the localization signal of galactosyltransferase and the functional catalytic domain of a fucosyltransferase.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Claims 48-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sandrin *et al.* (WO 95/34202) or Cooper *et al.* (6,331,658) with Sandrin *et al.* (Nature Med, Dec. 1995), Machamer (Curr. Opin. Cell Biol., 1993) and Sandrin *et al.*(Xenotransplantation, 1994).

Claims 48-53 encompass a method for reducing an amount of galactose (1,3) galactose present on cells comprising transducing a cell with a vector that encodes a chimeric enzyme comprising (1) a Golgi localization sequence, more specifically from the alph-1,3 galactosyltransferase and (2) a catalytic domain of a fucosyl transferase. Dependent claims set forth specific domains and sequences for each of these two embodiments of the vector that is transduced. Claims 54 and 55 encompass the same method of reducing galactose (1,3) galactose present on cells for the purpose of reducing the hyperacute rejection. The teaching of Sandrin *et al.*, Cooper *et al.*, Sandrin *et al.*, Machamer and Sandrin *et al.* as it applies to the polynucleotide sequence and vectors comprising a polynucleotide sequence that encodes a chimeric enzyme comprising (1) a Golgi localization sequence, more specifically from the alph-1,3 galactosyltransferase and (2) a catalytic domain of a fucosyl transferase is discussed above. With respect to using the vector in a method to reduce the amount of the HAR antigen (galactose (1,3) galactose) on cells, each of the references by Sandrin and Cooper specifically detail the problems of xenotransplantation specifically outlining the problems and possible solutions of HAR. Each detail the necessity of reducing the amount of HAR and provide experiments demonstrating that the expression of fucosyltransferase in the Golgi can effectively reduce the amount of an HAR on a cell in which it is expressed. Therefore, it would have been *prima facie*

obvious to one having ordinary skill in the art at the time the invention was made to provide a sequences that encodes a fucosyltransferase that when expressed would be present in the Golgi. Moreover, the reason provided by the cited references for providing and expressing such a sequence in a cell is to reduce the amount of HAR antigen, in particular in tissues used for transplantation. One having ordinary skill in the art would have been motivated to substitute the galactosyltransferase targeting domain onto a catalytically functional fucosyltransferase to provide for the same Golgi localization and more effective competition for the same carbohydrate acceptor. Further, the use of the vectors in methods to reduce the amount of HAR antigen in a xenogeneic transplant addresses one of the major shortcomings recognized in the art. There would have been a reasonable expectation of success given the level of skill in the art to use the polynucleotide sequences to reduce the amount of HAR antigen in a cell as evidenced by the working examples provided by both Sandrin and Cooper.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

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